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Paper 49
Filed: December 4, 2008

UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

FRANCIS **BARANY**,
GEORGE BARANY, ROBERT P. HAMMER,
Junior Party
(Application 09/986,527),

v.

GLENN H. **McGALL**,
CHARLES G. MIYADA, MAUREEN T. CRONIN,
JENNIFER D. TAN, and MARK S. CHEE
Senior Party
(Patent 6,156,501).

Patent Interference No. 105,351
(Technology Center 1600)

Before: RICHARD E. SCHAFER, SALLY G. LANE, and
MICHAEL P. TIERNEY, *Administrative Patent Judges*.

SCHAFER, *Administrative Patent Judge*.

DECISION - INTERLOCUTORY MOTIONS

Statement of the Case

Barany filed five motions (Barany Motions 2-6) attacking the patentability of McGall's claims and McGall's accorded benefit.

We have jurisdiction. 35 U.S.C. §§ 6(b) and 135(a).

McGall has neither filed oppositions nor filed any motions of its own.

We deny Barany's Motions 2 and 3 challenging McGall's accorded benefit. We grant Barany's Motion 4 and hold that the subject matter of McGall's involved claims is not supported by an enabling disclosure. In light of our decision on Barany's Motion 4 holding all McGall's involved claims unpatentable, it is unnecessary for us to reach Barany's Motions 5 and 6.

The Invention

The parties' invention relates to arrays for analyzing oligonucleotides in a solution. An array is a substrate having regions of selected oligonucleotide "probes." The oligonucleotide probes bind or "hybridize" to complementary oligonucleotide targets in the solution. Probe-target hybridization is usually detected and quantified by fluorescence-based detection of fluorophore-labeled targets. The intensity of the fluorescence signal identifies the relative abundance of the target nucleic acid sequences in the solution.

Such arrays have a variety of uses in medicine and molecular biology. For example, arrays may be used to identify a single nucleotide or base difference between different oligonucleotide targets mixed in the solution. Ex. 2001, p. 10, ¶ 19, ll. 3-7; Ex. 2003, col. 7, ll. 30-33.

The parties' invention uses modified oligonucleotides -- oligonucleotide analogues. Papers 7 and 12. An "oligonucleotide analogue" is an oligonucleotide which differs in sequence from a naturally occurring oligonucleotide but will still hybridize to the natural complement. Ex. 2003, col. 4, ll. 2-7; Barany Application, Specification, p. 40, ll. 37-38.

Barany's Motions

Barany's Substantive Motions 2 and 3 (Papers 30 and 31) challenge the accorded benefit of the filing date of McGall's parent application 08/440,742. The principal bases of attack is the parent application has neither written descriptive support nor an enabling disclosure for (1) arrays having "thousands of probes, " and (2) the requirement that the probes and targets have similar hybridization stability across the array. Barany's Substantive Motions 4 and 5 (Papers 32 and 33) allege that McGall's involved claims are unpatentable under 35 U.S.C. § 112, ¶ 1, because the specification of McGall's involved application lacks written descriptive support and an enabling disclosure for the similar hybridization stability limitation. Lastly, Barany's Substantive Motion 6 argues that "similar hybridization stability across the array" is indefinite.

Barany's Motions 2 and 3 Attacking McCall's Accorded Benefit

Barany's Motions 2 and 3 challenge the benefit accorded to McGall of the filing date of McGall's parent Application 08/440,742 for the subject matter of the count.

Principles of Law

A party to an interference is accorded the benefit of the filing date of an earlier application when that application provides a constructive reduction to practice of the subject matter of the count under 35 U.S.C. § 102(g)(1). 37 C.F.R. § 41.201, definition of "accord benefit." When interference priority is at issue, constructive reduction to practice of the subject matter of the count may be established by disclosure of one embodiment meeting all the limitations of the count. *Frazer v. Schlegel*, 498 F.3d 1283, 1287 (Fed. Cir. 2007); *In re Zletz*, 893 F.2d 319, 323 (Fed. Cir. 1989) (in an interference, "[p]riority as to a genus may be indeed shown by prior

invention of a single species . . . ."); *Fontijn v. Okamoto*, 518 F.2d 610, 617 (CCPA 1975) (foreign application disclosing one embodiment of the invention that meets the count as broadly construed, and that meets the requirements of 35 U.S.C. § 112, is sufficient to establish constructive reduction to practice).

During an interference each party's claims are construed in light of its own specification. 37 C.F.R. § 41.200(b) ("A claim shall be given its broadest reasonable construction in light of the specification of the application or patent in which it appears.)

As the moving party, Barany has the burden of proof. 37 C.F.R. § 41.121(b).

Issues

Barany argues, inter alia, that McGall's parent application does not describe or enable the subject matter of Barany's Claims 15, 25, 28, 35, 36, or 37 (hereinafter "Barany's count claims"). Paper 30, pp. 20-21; Paper 31, pp. 20-21. More specifically, Barany argues that all of McGall's claims require a "plurality of oligonucleotide analogue probes" and when used in the context of a nucleic acid detection array was understood by those skilled in the art as being an array that contains thousands of probes or more. Paper 30, p. 20, ll. 14-17; Paper 31, p. 20, ll. 18-21. According to Barany, McGall's parent application does not enable or describe arrays having thousands of probes. Paper 30, p. 20, ll. 17-19; Paper 31, p. 21, ll.1-3.

The issue raised by Barany's Motions 2 and 3 is whether Barany has proved that McGall's parent application does not enable or describe an embodiment within the scope of the count. In deciding this issue we must construe Barany's count claims and decide whether those claims require at least "thousands of probes." Stated another way, we must decide whether

Barany's count claims exclude arrays having fewer than "thousands of probes."

Analysis

Barany's asserts that McGall should not have been accorded the benefit of its parent application because McGall's parent application does not describe or enable arrays having "thousands of probes." Paper 30, p. 20, ll. 14-17; Paper 31, p. 20, l. 18 - p. 21, l. 1. According to Barany:

> the Barany claims all require a "plurality of oligonucleotide probes" comprising peptide nucleotide analogues or complementary to target nucleic acids comprising peptide nucleotide analogues. As shown above, "a plurality of oligonucleotide analogue probes" when used in the context of a nucleic acid detection array was understood by one skilled in the art at the time as encompassing an array that contained thousands of probes or more. The McGall [parent] application does not teach how to make or use the claimed arrays of thousands of probes. Therefore, it does not enable the Barany claims that all require an array with a plurality of oligonucleotide probes.

Paper 30, p. 20, ll. 12-19. <u>See also</u> Paper 31, p. 20, l. 16 - p. 21, l. 21 (making a similar statement with respect to written description).

The standard for benefit is set forth in the interference rules: "*Accord benefit* means Board recognition that a patent application provides a proper constructive reduction to practice under 35 U.S.C. 102(g)(1)." 37 C.F.R. § 41.201, definition of "accord benefit." An earlier application is a constructive reduction to practice of the subject matter of a "count" when that application describes and enables an embodiment within the scope of that count. *Frazer*, 498 F.3d at 1287; *Zletz*, 893 F.2d at 323; *Fontijn*, 518 F.2d at 617. Thus, in order to prove that McGall should not have been accorded the benefit of the filing date of McGall's parent application,

Barany must prove that the written description of that application does not describe or enable at least an embodiment falling within the scope of the count.

Count 1, the sole count of this interference, is:

> Any of claims 15, 25, 28, 35, 36, or 37 of Barany (09/986,527)
>
> **or**
>
> Any of claims 1, 26, 35, 51 or 58 of McGall (6,156,501).

Paper 1, p. 4. The subject matter of Count 1 encompasses every embodiment that meets all the limitations of any of the claims referenced by the count.[1] As Count 1 includes the subject matter of some of Barany's claims, Barany must prove that McGall's parent application does not describe or enable an embodiment within the scope of Barany's claims, as well as McGall's own claims.

Barany argues that McGall's written description neither describes nor enables arrays having "thousands of probes." Paper 30, p. 20, ll. 14-17;

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[1] The purpose of the count is to delineate the evidence which may be submitted to prove priority. *In re Van Geuns,* 988 F.2d 1181, 1183 (Fed. Cir. 1993); *Squires v. Corbett*, 560 F.2d 424, 433 (CCPA 1977). The subject matter of Count 1 is the sum of the subject matter of each of the claims referenced in the count. Although the count identifies this subject matter by incorporating certain claims of each party, the parties are not limited to submitting proof limited to the subject matter of their own claims. For example, McGall may submit proof of an actual reduction to practice of an embodiment falling within the scope of Barany's Claim 15 even if that embodiment would not be within the scope of any of McGall's claims. According benefit is similar. A description in the written description in McGall's parent application of an enabled embodiment within the scope of any of the Barany's claims entitles McGall to the benefit of the filing date of the McGall parent even if that embodiment would not be within the scope of any of McGall's claims.

Paper 31, p. 20, l. 18 - p. 21, l. 1. While Barany's claims require a plurality of oligonucleotide probes, none of Barany's claims expressly require any particular number of probes. Paper 7, pp. 4-7, Claims 15, 25, 28, 35, 36, and 37. Thus, for Barany to prevail on its motions, "plurality of oligonucleotide probes" as used in its count claims must be construed to exclude arrays having less than "thousands of probes." We must, therefore, construe Barany's count claims.

Construction of "Plurality of Oligonucleotide Probes"

During an interference each party's claims are construed in light of its own specification. 37 C.F.R. § 41.200(b) ("A claim shall be given its broadest reasonable construction in light of the specification of the application or patent in which it appears.") The claim terms are given the ordinary and customary meaning to a person skilled in the art.

Barany's Motions 2 and 3 do not direct us to anything in his specification or in the prosecution history which suggests that arrays having a "plurality of oligonucleotide probes" as used in Barany's count claims requires at least "thousands of probes." Barany has not directed us to an express definition in the written description, to any specific examples or to a clear disclaimer of claim scope. Instead, Barany relies on the testimony of Prof. John SantaLucia, Jr. Ex. 2001. The record establishes Prof. SantaLucia as an expert in the field of nucleic acid hybridization and in the design of nucleic acid probes for nucleic acid detection arrays. Ex. 2001, pp. 1-3, ¶ 1-6.

Based upon Prof. SantaLucia's testimony, Barany argues: "Arrays are <u>typically</u> constructed with anywhere from thousands to one million or more different probes present on the array..." Paper 30, p. 3, ll. 8-12; Paper 31, p. 3, ll. 5-8 (emphasis added). Prof. SantaLucia states that "conventional"

arrays have a large number of probes and <u>may be</u> constructed with "thousands to a million or more probes:"

> Conventional arrays have a large number of probes bound to the solid surface in a spatially segregated manner, like a large chess board . . . This construction permits anywhere from thousands to a million or more different probes to be present on the array, with each one at a known location or spot.

Ex, 2001, ¶ 17.

Prof. SantaLucia's testimony does not support the proposition that Barany's count claims exclude probes having less than "thousands of probes." His testimony only establishes that Barany's claims would be understood to encompass arrays with "thousands of probes." His testimony does not establish that one skilled in the art would understand the claims to exclude arrays having less than "thousands of probes."

Giving Barany's count claims their broadest reasonable construction, those claims encompass arrays having thousands to millions of probes but also encompass arrays having a much smaller number of probes.

McGall's Accorded Benefit

Barany's arguments and proofs assert that McGall's parent application does not describe or enable arrays having thousands or more probes. However, since Barany's claims are not limited to arrays having at least thousands of probes, Barany's arguments relating to description and enablement of arrays with thousands of probes, even if true, are insufficient to strip McGall of its accorded benefit. Barany has failed to prove that McGall's written description does not describe or enable an embodiment having fewer than "thousands of probes."

Barany also argues that his count claims require "uniform hybridization conditions" and McGall's parent application does not enable or describe this limitation. Paper 30, p. 20-21; Paper 31, p. 21.

While Barany's claims require "uniform hybridization conditions," McGall has neither explained the basis for the asserted lack of enablement, nor directed us to evidence in support. Thus, Barany has presented only attorney argument. Attorney argument can not take the place of evidence in the record. *Estee Lauder Inc. v. L'Oreal, S.A.,* 129 F.3d 588, 595 (Fed. Cir. 1997).

Conclusion of Law

Barany has failed to prove that the written description of McGall's parent application does not describe or enable an embodiment within the scope of Barany's Claims 15, 25, 28, 35, 36, or 37.

Barany's Motions 2 and 3 are denied.

Barany's Motion 4 Asserting McGall's Involved Claims Are Not Enabled

Barany's Motion 4 asserts that McGall's involved claims are not supported by an enabling disclosure. In McGall's claims, either the probes or targets are analogues. Additionally, all of McGall's claims either expressly require or encompass arrays in which each probe oligonucleotide has a different sequence. For example, McGall's Claim 26 requires "an array of a plurality of oligonucleotide probes having different sequences . . . ." All of McGall's claims also require that the different probes bind to oligonucleotide targets "with a similar hybridization stability across the array."

According to Barany, this limitation requires that the stability of the analogue oligonucleotide hybrids be about the same for all the hybrids on

the array and that McGall's written description does not enable such arrays for the full scope of McGall's claims.

Issues

The issues raised by Barany's Motion 4 are (1) what is the meaning of "similar hybridization stability across the array" in the context of McGall's claims and (2) whether Barany has proved that McGall's written description does not enable arrays having a plurality of different probes where the stability of the analogue oligonucleotide hybrids be about the same for all the hybrids on the array.

Construction of "Similar Hybridization Stability Across the Array"

The phrase itself is not difficult to decode. Applying the literal meanings to the words, "similar" means about the same, "hybridization stability" means the tendency of the probe-target hybrids to remain as hybrids or to separate; "across the array" means throughout or in the entire array. Thus the limitation requiring that the probes and targets bind with a similar hybridization across the array literally means that tendency of the probe-target hybrids to remain bound or to separate is about the same for all the probe-target hybrids in the array.

Of course we must look to McGall's written description to see if a different connotation has been given. Unfortunately, neither the phrase itself nor the terms "hybridization stability" or "across the array" are used in McGall's written description. The phrase was apparently added to the claims by amendment during prosecution of the application. Application 08/630,427, Paper 30, entered December 20, 1999.

We note, that while "hybridization stability" does not appear, McGall's written description uses the phrase "duplex stability." A "duplex"

is a hybrid formed by two single nucleotide strands. Ex. 2001, p. 13, ¶ 25, ll. 18-19. Our review of McGall's written description does not reveal any disclosure which would suggest the limitation has a meaning different than that conveyed by the literal meaning of the phrase "hybridization stability." Accordingly, we consider "hybridization stability" and "duplex stability" to be synonymous.

Barany again relies on the testimony of Prof. SantaLucia, Ex. 2001. He testifies that he reviewed McGall's patent. Ex. 2001, p. 3, ll. 8-10. Prof. SantaLucia testifies that he was asked to evaluate "what the term 'similar hybridization stability across the array' would mean to a scientist in the field of oligonucleotide array design." Ex. 2001, p. 6, ¶ 9, ll. 6-8. Prof. SantaLucia says that he did not find an explanation of that phrase in McGall's disclosure. Ex. 2001, p. 24, ¶ 45, ll. 21-23. Prof. SantaLucia further testified that "hybridization stability" refers to the amount of duplex that remains bound as a hybrid compared with the amount remaining in the unhybridized state under the particular hybridization conditions. Ex. 2001, p. 19, ll. 15-18. He testifies that the phrase "similar hybridization stability across the array" means

> to select and use oligonucleotides and oligonucleotide analogues in the probes and targets to obtain, across the whole array, the result of having similar hybridization stability for each probe and its intended target.

Ex. 2001, p. 24, l. 23 - p. 25, l. 3. He testifies that an array with similar hybridization stability across the array would display a fluorescence signal intensity that was substantially uniform across the array notwithstanding the use of different probes and a mixture of different targets. Ex. 2001, p. 25, ll. 6-8.

Prof. SantaLucia's testimony as to the meaning of "similar hybridization stability across the array" is consistent with the literal meaning we stated above.

Considering the evidence and the testimony, we construe the limitation requiring that a plurality of different probes bind to complementary targets with "similar hybridization stability across the array" to mean that the tendency of the probe-target hybrid to remain as a hybrid or to separate is about the same for all the probes and their respective targets on the array.

Enablement of "Similar Hybridization Stability across The Array"

Barany's Motion 4 argues that McGall's written description does not provide an enabling disclosure sufficient to teach one skilled in the art how to make or use arrays where the oligonucleotide probes or their oligonucleotide targets contain an oligonucleotide analogue and the duplexes formed have similar hybridization stability across the array. Paper 32, p. 1, ll. 15-19.

In the written description, McGall explains the use of analogues rather than naturally occurring oligonucleotides. McGall notes that analogues have different hybridization properties than the naturally occurring oligonucleotides. Ex. 2003, col. 1, ll. 53-55. According to McGall, these differences can be used to optimize hybridization with the targets. Ex. 2003, col. 1, ll. 55-58. The use of an analogue is also said to enhance or decrease hybridization stability while maintaining hybrid specificity. Ex. 2003, col. 7, ll. 50-62. McGall's written description also discusses specific analogues to increase or decrease hybridization stability. Ex. 2003, col. 8, l. 29 - col. 10, l. 2.

McGall describes techniques for verifying altered hybridization stability. Ex. 2003, col. 10, ll. 3-34. According to McGall, altered hybridization stability may be verified by monitoring fluorescent signal intensity of the arrays over time. More stable hybrids are said to generate higher signal intensity faster than less stable hybrids. Ex. 2003, col. 10, ll. 7- 2.

While McGall's written description notes that the use of analogues will change the hybridization stability and other characteristics, our review of the written description does not reveal any discussion relating to how to obtain or use arrays where the different probes or their targets are analogues and all the different duplexes formed have a similar hybridization stability.

Barany again relies on its expert, Prof. SantaLucia. He testifies that he was asked whether the McGall patent would have enabled "a skilled scientist in the field of array design" to make and use the arrays and methods claimed in the McGall patent as of April 3, 1996, the filing date of the application which matured into McGall's involved patent. Ex. 2001, p. 6, ¶ 9, ll. 9-12.

Prof. SantaLucia testifies that it took extensive experimental data to develop the techniques for the design and selection of probes used in arrays and those techniques did not become available in the public literature until December, 1996, after McGall's involved application was filed. Ex. 2001, p. 31, ¶ 56. He notes that the necessary techniques are not described in McGall's written description. Ex. 2001, p. 31, ¶ 56, ll. 18-21.

Prof. SantaLucia notes that in the 1995-1996 time frame, the effects of using nucleic acid analogues in arrays were unknown. Ex. 2001, p. 29, ¶ 54. He testifies that the specification does not teach how to obtain an array with

nucleic acid analogues and which are selected to bind targets with similar hybridization stability across the array. Ex. 2001, p. 29, ¶ 52.

He testifies that in oligonucleotide arrays having different probes, the probes will bind to their respective targets with different hybridization stability. Ex. 2001, p. 15, ll. 10-11. He testifies that multiple probe arrays used with a mixture of different targets normally display a wide range of signal intensities across the array. Ex. 2001, p. 25, ll. 8-9. On the other hand, an array with similar hybridization stability across the array would display a signal intensity that was substantially uniform across the array notwithstanding the use of different probes and a mixture of targets. Ex. 2001, p. 25, ll. 6-8.

He notes and details a number of factors one skilled in the art would have needed to know to achieve similar hybridization across the array. Ex. 2001, pp. 30-31, ¶ 55. Those factors included: (i) the surface effects of arrays, (ii) the sequence dependence of synthesis quality for probes or targets that contain analogues, (iii) sequence dependent binding biases, (iv) loading density effects, (v) secondary structure analyses of probe and target, (vi) which specific analogues to use in a probe or target, (vii) how many analogues to use in each single probe or target, (viii) where to use analogues in each probe or target, (ix) the positional dependence of the effects of nucleotide analogues (i.e., at a mismatch site, adjacent to a mismatch site, at a terminal site, at an internal site, etc.), and (x) the effects of nucleotide analogues on probe or target folding. Ex. 2001, pp. 30-31, ¶ 55. Prof. SantaLucia testified that such necessary guidance was missing from the McGall's written description. Ex. 2001, p. 31, ll. 3-4. He then testifies that the disclosure provides no rules or guidance for designing such arrays. Ex. 2001, p. 32, ¶ 57.

Prof. SantaLucia testified that he also reviewed the examples found in McGall's involved patent. Ex. 2001, pp. 32-40, ¶¶ 58-67 and 69-79. He testified that the examples provide no guidance that would allow a skilled scientist to design and use an array with similar hybridization stability across the array. Ex. 2001, p. 32, ¶ 57, ll. 7-8.

Based on his review he expressed the opinion that the written description provided inadequate data to predict hybrid stability. Predicting hybrid stability is said to be necessary to achieve similar hybrid stability for all the probes in the array:

> There is insufficient data to derive the parameters needed to properly model array hybridization to allow accurate predictions of hybridization stability, certainly not to the degree needed to achieve similar hybridization stability across the array.

Ex. 2001, ¶ 68, p. 36, ll. 1-4.

Prof. SantaLucia also concluded that Barany's written description did not teach one skilled in the art how to make and use an array in which the different probes had the similar hybrid stability with their respective targets:

> the description of the invention and the provided examples do not describe or teach how to make and use an "array" as claimed, namely one that contains a plurality of probes selected to bind to different targets (*i.e.*, a mixture of targets) with ***similar hybridization stability across the array***. The specification may discuss factors to be concerned about, but it completely fails to teach or describe how to achieve the required ***similar hybridization stability across the array***. The specification simply describes a goal without describing or teaching how to get there . . . .

Ex. 2001, p. 40, ¶ 81 (emphasis original).

Principles of Law

"To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993)). In deciding whether a disclosure teaches how to make and use the claimed subject matter without undue experimentation we may consider the "Wands factors:" (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Enzo Biochem Inc. v. Calgene Inc.*, 188 F.3d 1362, 1371 (Fed. Cir. 1999); *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). It is not necessary, however, to review all of the Wands factors in determining whether a disclosure is enabling. *Amgen, Inc. v. Chugai Pharm .Co., Ltd.*, 927 F.2d 1200, 1213 (Fed. Cir. 1991) (noting that the Wands factors "are illustrative, not mandatory. What is relevant depends on the facts.").

Analysis

Wands Factors

Experimentation

With respect to the quantity of experimentation necessary to obtain similar hybridization stability across the array, Prof. SantaLucia testified that extensive trial and error data was necessary to select suitable probes and that general rules for selecting probes were not reported until after the filing date of the McGall application which matured into McGall's patent. Ex. 2001, ¶ 56. Additionally, at the time that application was filed, the effect of

oligonucleotides analogues on arrays was not known. Ex. 2001, p. 29, ¶ 54, ll. 17-18.

We find that the quantity of experimentation necessary to make array employing oligonucleotide analogues and having similar hybridization stability across the array to be extensive.

Guidance and Examples in the Written Description

With respect to the amount of direction and guidance presented and the presence of examples, Prof. SantaLucia testified that in order to achieve similar hybridization stability across the array a person skilled in the art would need to know: (i) the surface effects of arrays, (ii) the sequence dependence of synthesis quality for probes or targets that contain analogues, (iii) sequence dependent binding biases, (iv) loading density effects, (v) secondary structure analyses of probe and target, (vi) which specific analogues to use in a probe or target, (vii) how many analogues to use in each single probe or target, (viii) where to use analogues in each probe or target, (ix) the positional dependence of the effects of nucleotide analogues (i.e., at a mismatch site, adjacent to a mismatch site, at a terminal site, at an internal site, etc.), and (x) the effects of nucleotide analogues on probe or target folding. Ex. 2001, pp. 30-31, ¶ 55. Prof. SantaLucia testified that such guidance was missing from the McGall written description. Ex. 2001, p. 31, ll. 3-4.

Our review of the written description reveals little or no information on these matters.

McGall's written description includes a number of examples. Prof. SantaLucia testified that he evaluated the examples. Ex. 2001, p. 36, ll. 19-20. After testifying as to each example he concluded that they do not provide the information necessary to make and use an array containing a

plurality of probes selected to bind to different targets with similar hybridization stability across the array. Ex. 2001, p. 40, ¶¶ 80 and 81.

Our review of the examples confirms that they do not provide information on making arrays using analogue probes or targets which bind with similar hybridization stability across the array.

We find that the written description and examples provide little guidance or direction as to making arrays employing the hybridization of a plurality of different probes which bind to a mixture of targets with similar hybridization stability for each of the target/probe duplexes.

Unpredictability, Level of Skill in the Art and State of the Prior Art

Prof. SantaLucia testified that the effects of oligonucleotide analogues in arrays were unknown at the time the McGall application was filed. Ex. 2001, p. 29, ¶ 54, ll. 17-18. He additionally testified that at the time the McGall application was filed, development of useful arrays required development of extensive experimental data. Ex. 2001, p. 31, ¶ 56. Techniques to simplify development were not reported until after McGall's filing date. Ex. 2001, p. 31, ¶ 56, ll. 7-18. He testified that

> There is insufficient data to derive the parameters needed to properly model array hybridization to allow accurate predictions of hybridization stability, certainly not to the degree needed to achieve similar hybridization stability across the array.

Ex. 2001, ¶ 68, p. 36, ll. 1-4.

We find that at the time the McGall application was filed the development of useful arrays was unpredictable, that the routine skill of those working in the oligonucleotide array art and the state of the prior art was insufficient to make useful arrays using oligonucleotide analogues in

which the target/probe stability was about the same for all the probes in the array.

Scope of the claims

McGall's claims encompass all arrays employing any oligonucleotide analogues as probes or targets in which the hybridization or binding stability is about the same for each complementary probe-target combination in the array notwithstanding that there are multiple probes and targets having different sequences. The claims cover millions of possible probe-target combinations. Thus, McGall's claims are very broad in scope.

Additional Evidence

In addition to the Wands factors we have also considered Prof. SantaLucia's testimony that McGall's written description did not teach one skilled in the art how to make and use an array in which the different probes had similar hybrid stability:

> the description of the invention and the provided examples do not describe or teach how to make and use an "array" as claimed, namely one that contains a plurality of probes selected to bind to different targets (*i.e.*, a mixture of targets) with ***similar hybridization stability across the array***. The specification may discuss factors to be concerned about, but it completely fails to teach or describe how to achieve the required ***similar hybridization stability across the array***. The specification simply describes a goal without describing or teaching how to get there . . . .

Ex. 2001, p. 40, ¶ 81 (emphasis original).

The record establishes Prof. SantaLucia as an expert in the art. His testimony was neither cross-examined nor rebutted. We credit his testimony.

Conclusions of Law

We hold that each of the relevant Wands factors favors a conclusion that undue experimentation would have been necessary to make and use arrays in which the probes or targets include oligonucleotide analogues in which the hybridization stability was similar across the array. Accordingly, we conclude that Barany has proven that undue experimentation would have been necessary to practice the subject matter of McGall's claims.

The record including Prof. SantaLucia's testimony establishes, prima facie, that McGall's written description did not provide an enabling disclosure sufficient to teach one skilled in the art how to make arrays where different oligonucleotide probes or their oligonucleotide targets are oligonucleotide analogues and the duplexes formed have similar hybridization stability across the array for the full scope of the claimed subject matter. *Genentech*, 108 F.3d at 1365; *Wright*, 999 F.2d at 1561 ("To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'").

We grant Barany's Motion 4. McGall's involved Claims 1-72 are unpatentable under 35 U.S.C. § 112, ¶ 1.

Barany's Other Motions

Because we have held all of McGall's involved claims unpatentable, it is not necessary for us to reach Barany's Motions 5 and 6 asserting that McGall's claims are not supported by a written description and are indefinite, respectively.

Barany's Motions 5 and 6 are dismissed.

Order

Barany Motion's 2 and 3 (Papers 30 and 31) are denied.

Barany Motion 4 (Paper 32) is granted.

Barany Motions 5 and 6 (Papers 33 and 34) are dismissed.

/Richard E. Schafer/	)	
RICHARD E. SCHAFER	)	
Administrative Patent Judge	)	
	)	
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